TECHNICAL SERVICES DEPT QUARTERLY REVIEW

Minimum Ignition Energy

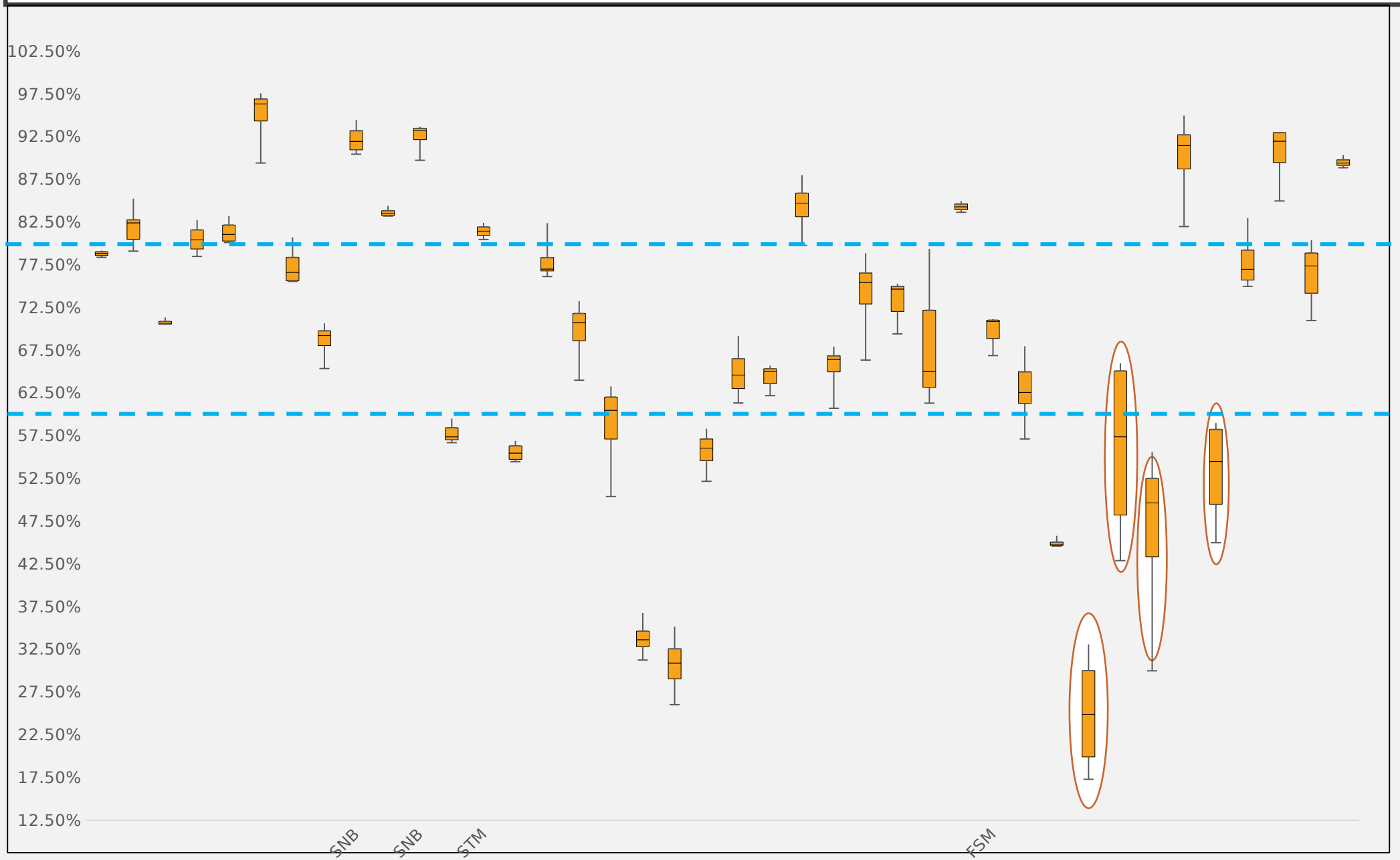
The **minimum ignition energy** (MIE) is a safety characteristic in explosion protection and prevention which determines the ignition capability of fuel-air mixtures, where the fuel may be combustible vapor, gas or dust. It is defined as the minimum electrical energy stored in a capacitor, which, when discharged, is sufficient to ignite the most ignitable mixture of fuel and air under specified test conditions.[1] The MIE is one of the assessment criteria for the effectiveness of ignition, e.g. the discharge of electrostatic energy, mechanical ignition sources or electromagnetic radiation. It is an important parameter for the design of

Capacitance

Body capacitance is the physical property of the human body that it acts as a capacitor. Like any other electrically conductive object, a human body can store electric charge if insulated.

Synthetic fabrics and friction can charge a human body to about 3 kV.
Notably, a combination of footwear with some sole materials, low humidity, and a dry carpet (synthetic fiber in particular) can cause footsteps to charge a person's body capacitance to as much as a few tens of kilovolts with respect to the earth. The human and surroundings then constitute a highly charged capacitor. A close approach to any conductive object connected to earth (ground) can create a

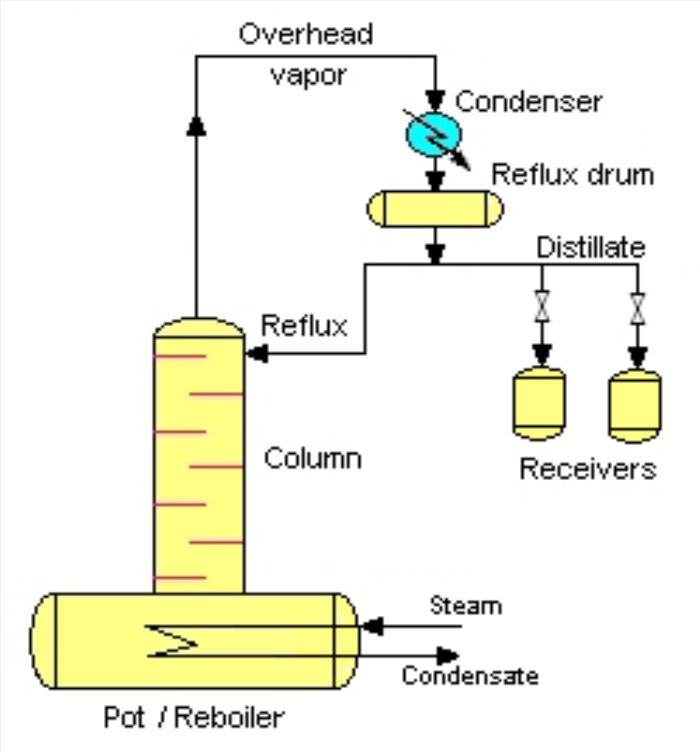
YIELD TREND AND CONSISTENCY DURING NEW PRODUCT SCALE-UP



- ~40% of the products scaled up have yields in-between 60-80%.
- ~32.5% of the stages yields are higher 80%.
- ~27.50% of the product yields are lower than 60%.
- The lower range attributed from products like Pemegatinib, Remigepant. Lumetoperone, etc.
- As an industry benchmark, we have to improve by 10% in yield from the current level.

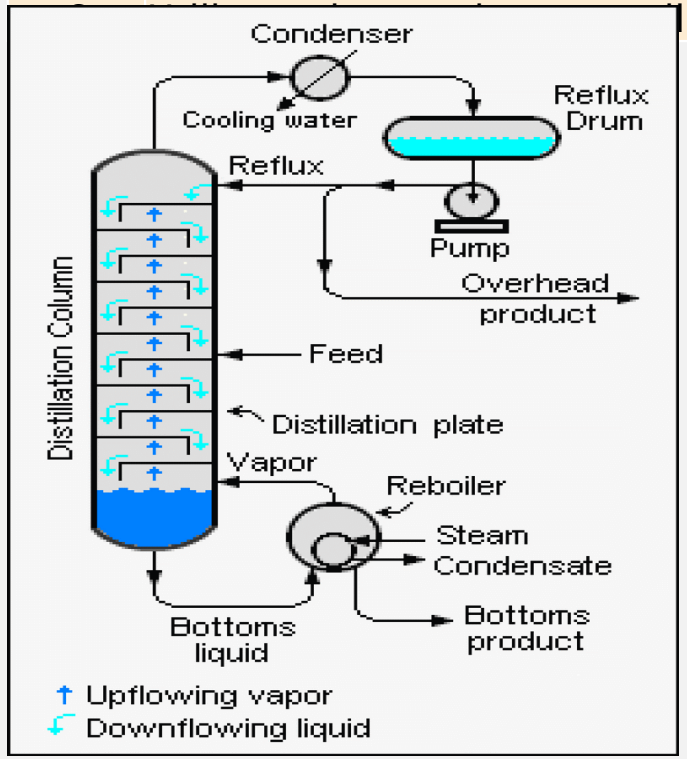
Existing Solvent Recovery System (Batch columns)

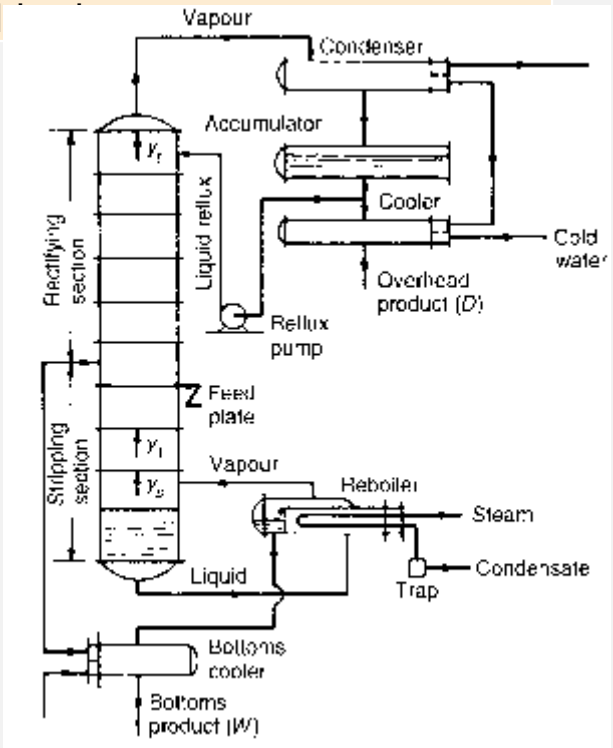
1	Existing Solvent recovery is for only batch column
2	With out adequate automation - Safety interlocks & process controls
3	Can be utilize only for top collections
4	Can be handled only up to 150 - 200 KL spent/month
5	Batch cycle time is more and recovery percentage is lower side
6	Utility and operating cost is more



Proposed Solvent Recovery System (With Continuous top & bottom collections)

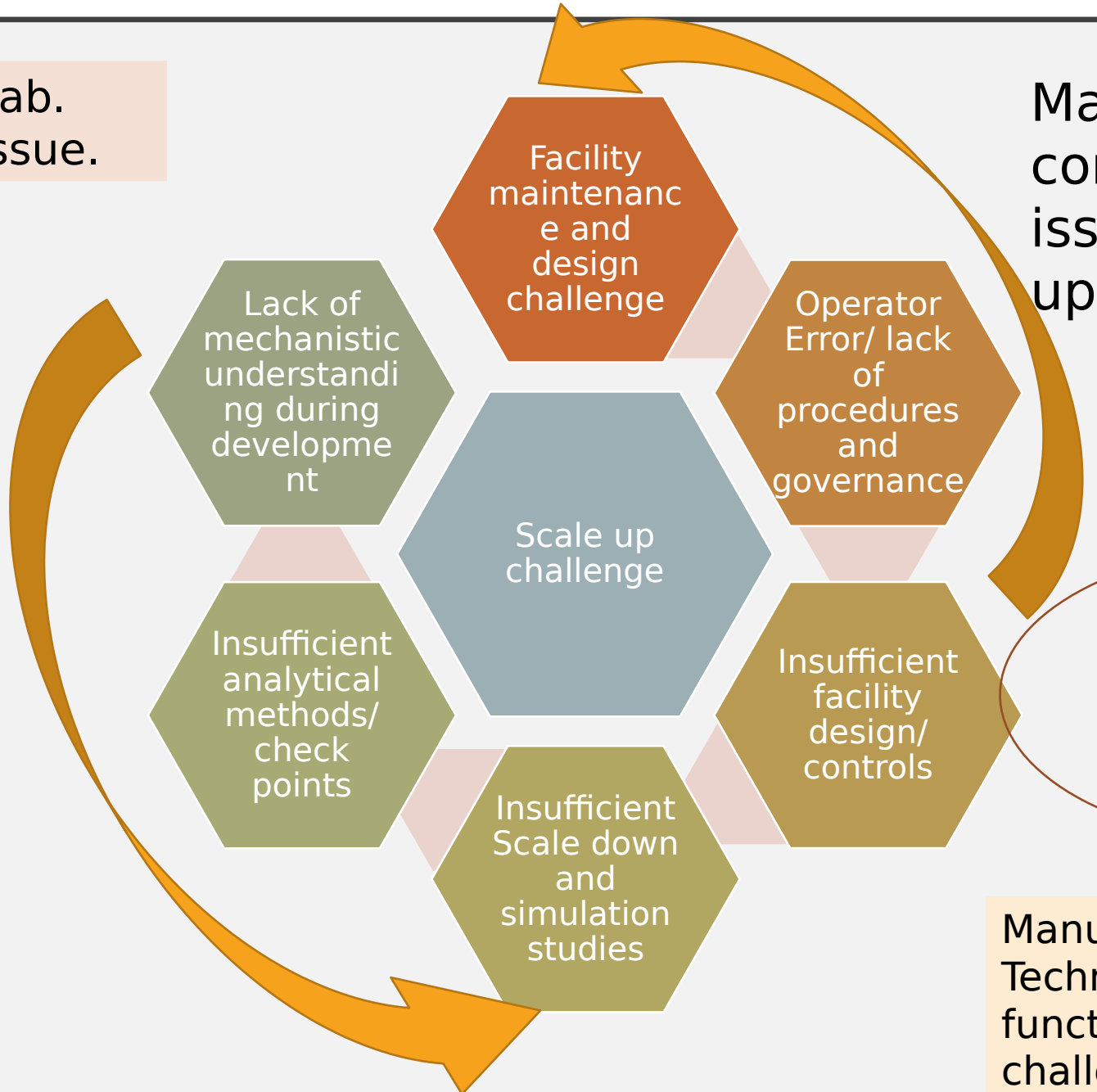
1	Modified column can be used for both batch, continuous and semi continuous
2	Adequate automation - Safety interlocks & process controls were considered
3	Can be utilize for both top collections & Bottom collections
4	Can be handled up to 300 - 500 KL spent/month
5	Batch cycle time will be less and recovery percentage will be higher side





WHAT IS A SCALE-UP ISSUE?

I don’t see it in lab.
It is a scale up issue.


Facility maintenance and design challenge
Operator Error/ lack of procedures and governance
Insufficient facility design/ controls
Insufficient Scale down and simulation studies
Insufficient analytical methods/ check points
Lack of mechanistic understanding during development
Scale up challenge

Manufacturing component to issues in scale up.

Science component to issues in scale up.

Technology component to issues in scale up.

Manufacturing, Science and Technology – An evolved function to address scale up challenge

PROCESS ENGINEERING INTERVENTION DURING EARLY DEVELOPMENT

CASE STUDIES

INITIATIVES FOR PROCESS ROBUSTNESS AT SCALE

Scale-down approach for negative data generation

- Structured approach to understand the SD and SI parameter interactions.
- Simulating the mixing profiles at both scales and generate equivalence.
- Generate data at lab for all unit operations and use the correlations to design the facility.
- Generate base line performance at lab and kilo lab.

Right facility for consistant performance

- Secondary heating / cooling utility for sensitive reactions
- Identifying critical equipment set-up well before TT.
- Controlled storage / powder handling areas for critical molecules.

Predictive Scale-up Approach

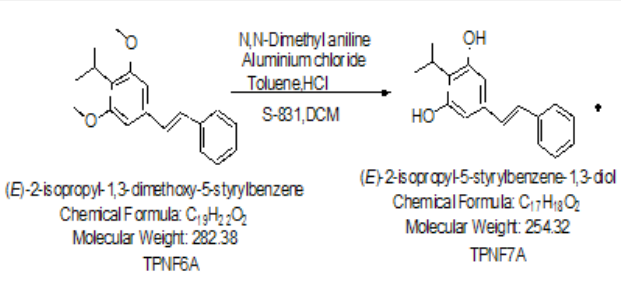
- Standardized data generation at lab for all the unit operations and compare against the plant performance.
- Process and facility FMEA to identify the facility risk at plant.

Safety emphasis

- Process Safety evaluation (RC and Powder characteristics) to identify process risk and also use as optimization tool.

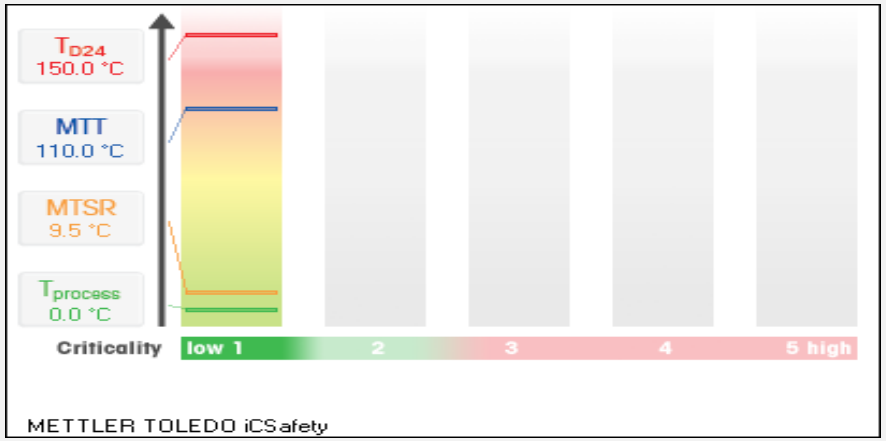
THERMAL RISK ANALYSIS BY REACTION CALORIMETER

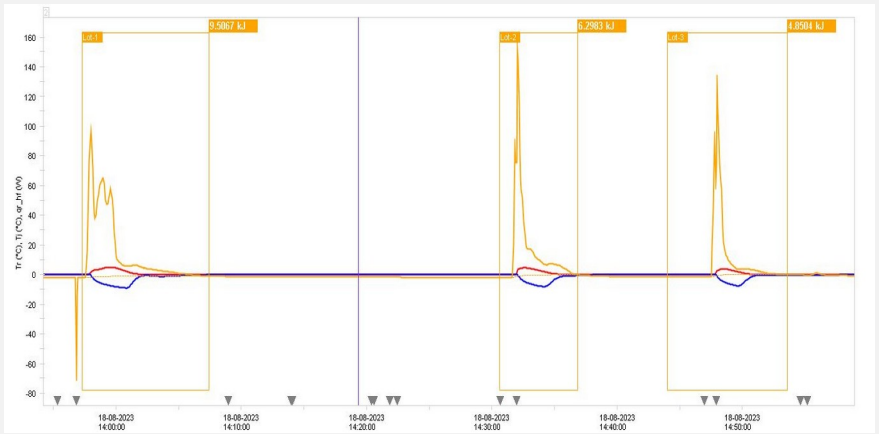
Dimethylation step of Tapinarof Product

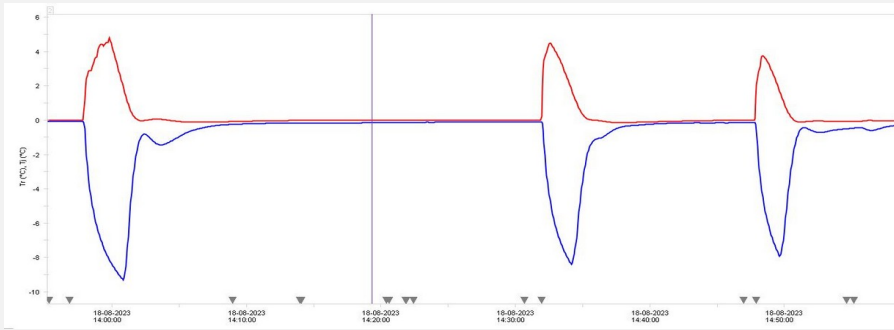


- TPNF6A starting material
- Toluene as Solvent
- Dimethyl aniline
- Addition of Aluminium

Reaction calorimetry Set-up

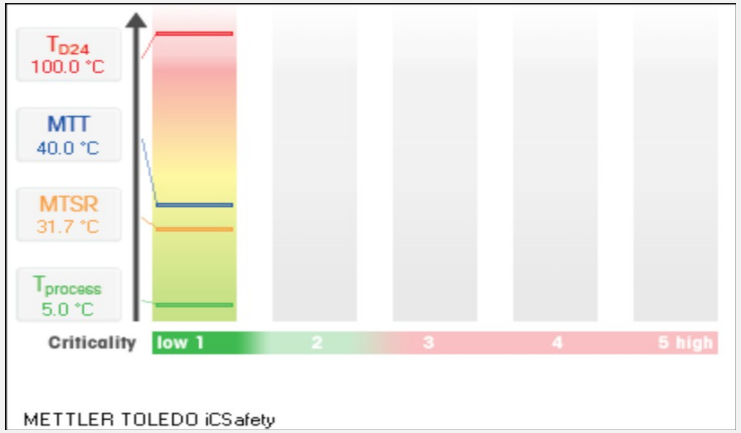




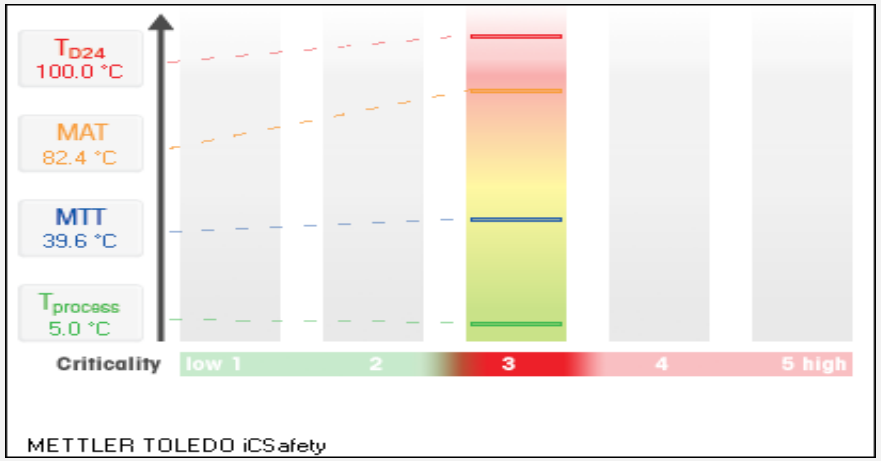


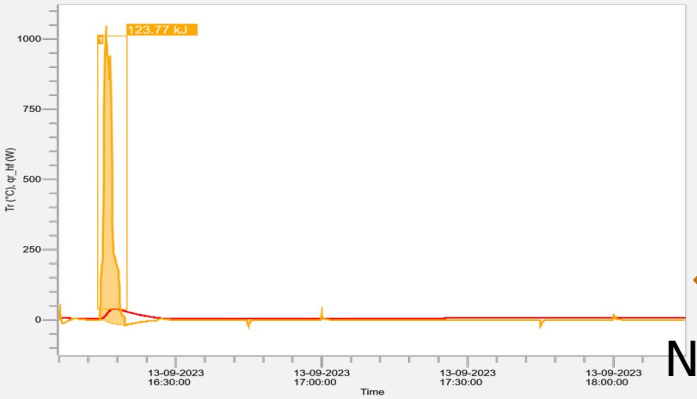
Material	AlCl3 Lot-1	AlCl3 Lot-2	AlCl3 Lot-3
Process Temperature	0°C		
Adiabatic temperature raise	14.75	8.91	6.94
Maximum Temperature of Synthetic reaction	14.75°C		
Thermal accumulation at the end of dosing	10%	10%	10%
Stoessel's criticality index	Class-1 (MTT > MTSR > ΔTad)		

THERMAL RISK ANALYSIS BY REACTION CALORIMETER

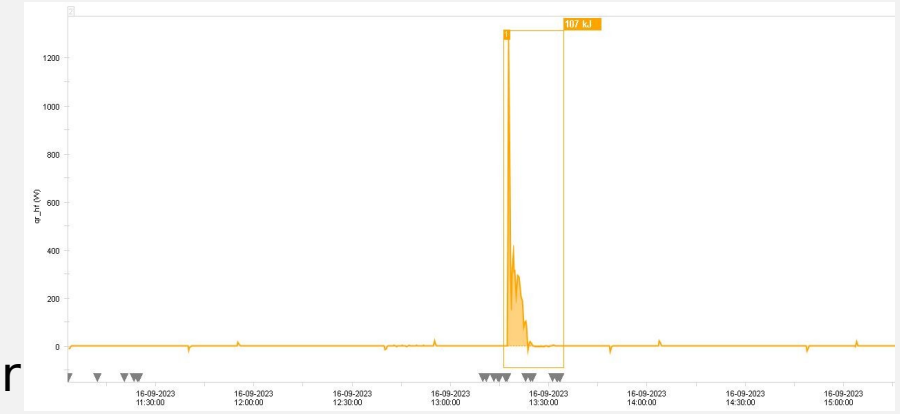


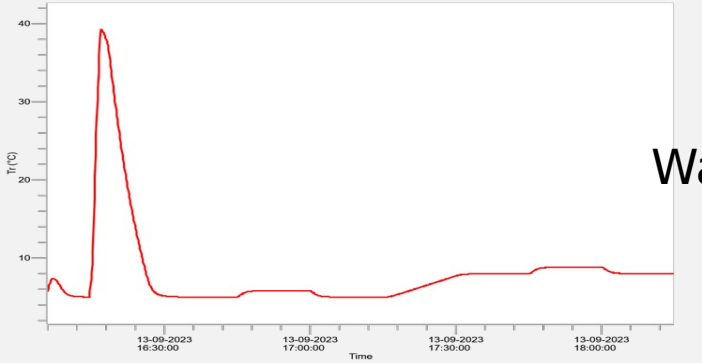
Reaction calorimetry Set-up



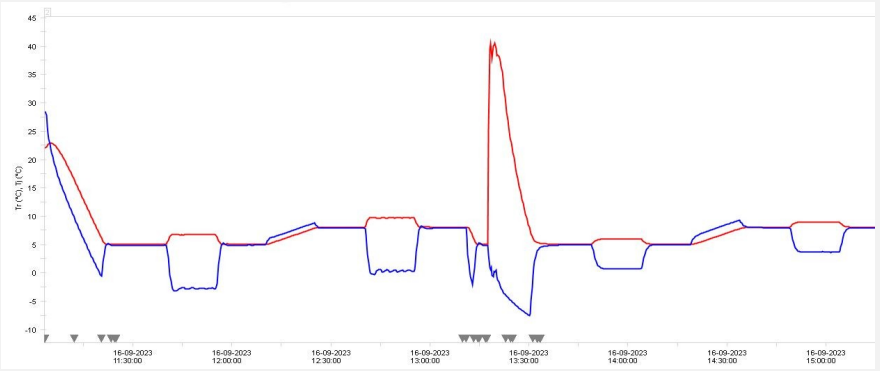


Nitration reaction mass addition to water



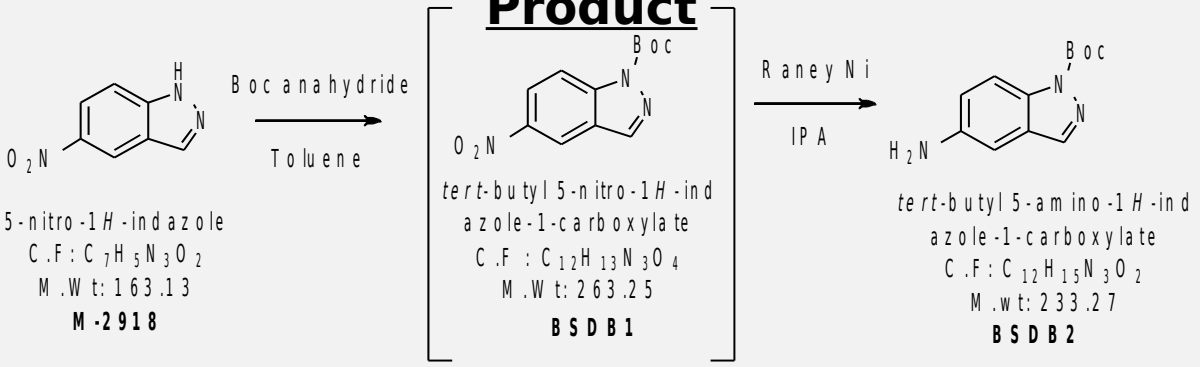


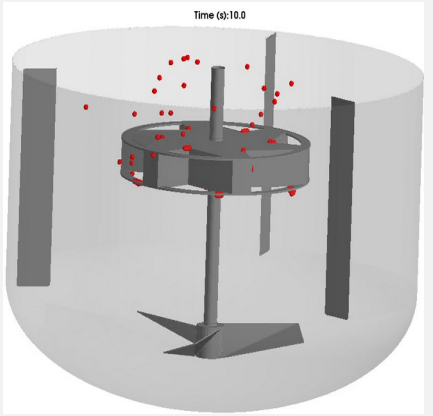
Water addition to nitration reaction mass



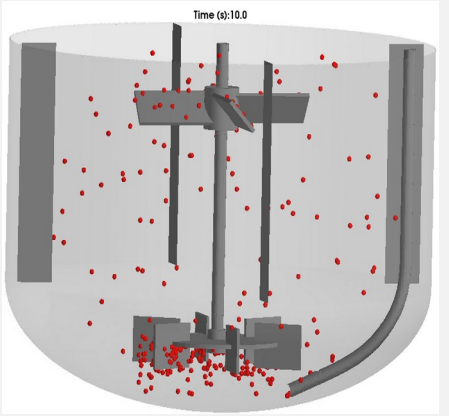
MIXING SIMULATION – FOR REACTION - CASE STUDY 1

Hydrogenation in BLSB1 stage of Belumosudil Product





Kilolab Hydrogenator



Organics Plant Hydrogenator

Reactor	Hydrogenation time	Amino deboc impurity
Lab	~1 hour	0.45%
Kilolab	~4 hours	0.66%
Plant	~ 30 min	0.18%

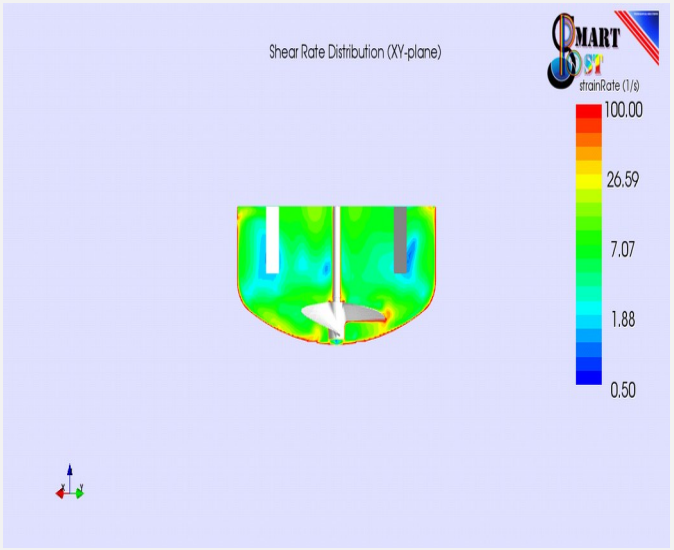
Predictive scale-up using mixing simulation software.

Parameter	Unit	Kilo-lab	Plant
Total Power Consumption	kW	0.0131	0.2287
Power Per-Unit Volume	kW/m3	0.2188	0.3472
Average Strain Rate	1/s	13.9746	9.2509
Volume Average TDR	m2/s3	0.2224	0.3698
Micromixing time calculated based on Average TDR (epsilon)	s	0.0407	0.0315
Average Bubble Size	m	0.0066	0.003
Gas-Liquid Mass Transfer Coefficient	1/hr	9.8927	20.4229

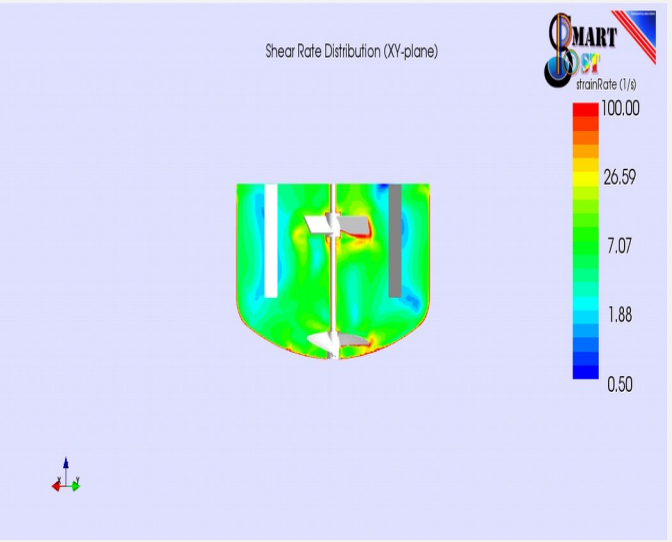
MIXING SIMULATION FOR CRYSTALLISATION – CASE STUDY 2

Crystallisation in ISVS4 stage of Isavocanazonium Sulfate Product

- The Crystallisation is critical with respect to %occupancy, removal of Acetonitrile to ICH limits (NMT 410 PPM).
- Excess drying in order to remove Acetonitrile leads to Alcohol impurity formation thereby failing w.r.t quality.
- Outcome of the plant batch predicted well before execution with mixing simulation.

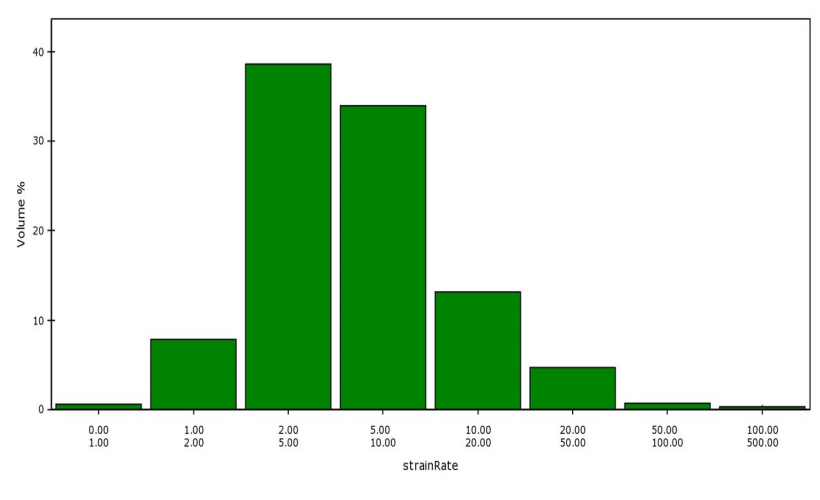


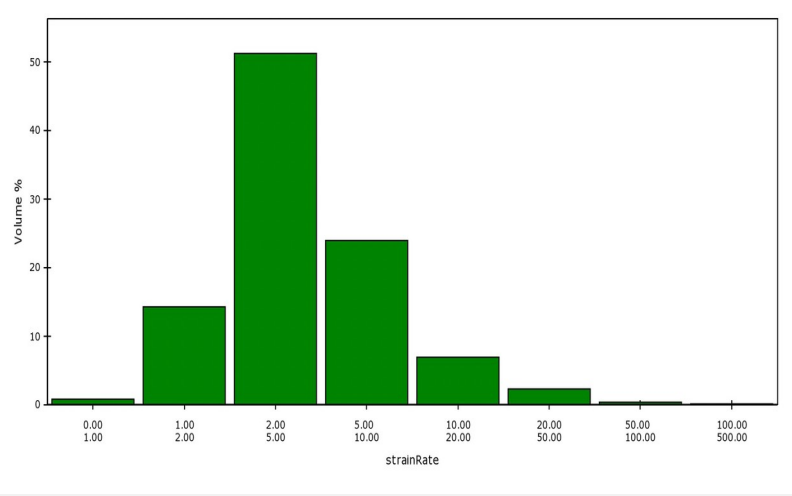
Kilolab Reactor



LS-II Plant

Reactor	Drying time	ACN by GC	Alcohol Impurity (%a/a)
Kilolab	9-12 hours	<200 PPM	0.2%
Plant	12-15 hours	<200 PPM	~0.3%





Shear rate Distribution

PROCESS ENGINEERING INTERVENTION DURING EARLY OPTIMISATION – CASE STUDY- LERCANIDIPINE HCL

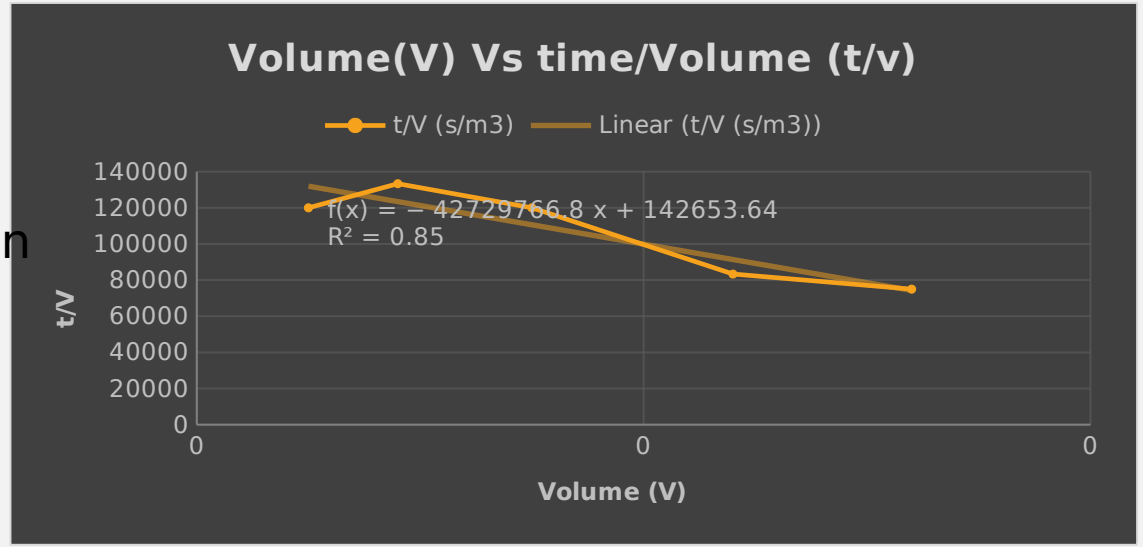
Operation	Initial Process	Modified	Rational / Benefits
Condensation & cyclization reaction	S-820 - 2V 3-Nitrobenzaldehyde - 1.0 eq. Tertiary butyl acetoacetate - 2.0 eq.	S-820 - 5V 3-Nitrobenzaldehyde - 1.0 eq Tertiary butyl acetoacetate - 1.3 eq	Challenge: Boiling point of Tertiary butyl acetoacetate is 156oC. Removal of excess tertiary butyl acetoacetate is a challenge Benefits with the changes: • Reduced reaction time • Avoidance of distillation • Cost and time cycle reduction
	Reaction maintaining at 80±5°C 40 -42 hrs	Reaction maintaining at 85±5°C for 35 hours	
	S-820 distillation under vacuum at below 80°C, followed S-820 co-distillation.	Excluded distillation and co-distillation operation	

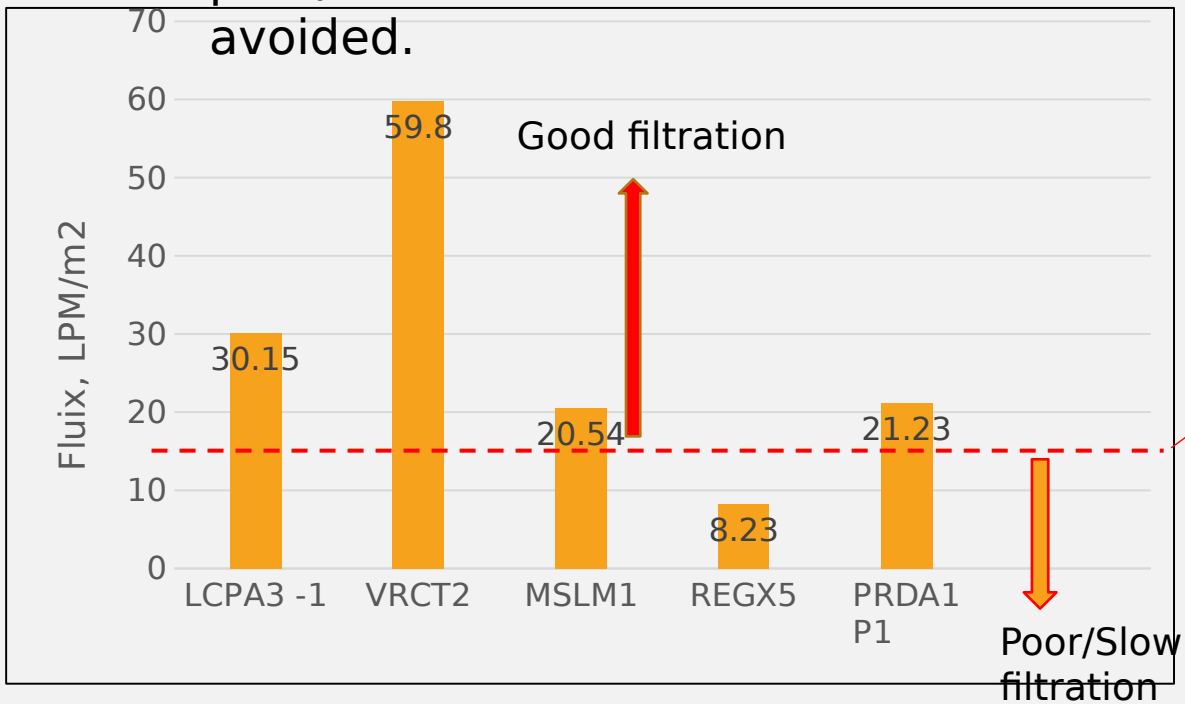
FILTRATION OPTIMISATION – WAY FORWARD

Pocket Filter for Filtration studies

- All the new processes / products are assessed for the filtration flux.
- These studies help in selection of filtration equipment during scale-up.
- Also issues such as improper wash ability / solvent trapping due to poor/bad filtration can be avoided.

Filtration studies





Flux	Decision Point
> 20 LPM/m2	Good filtration and can be proceeded further
< 20 LPM/m2	Slow / Poor filtration and process needs to be relooked

Thank you!

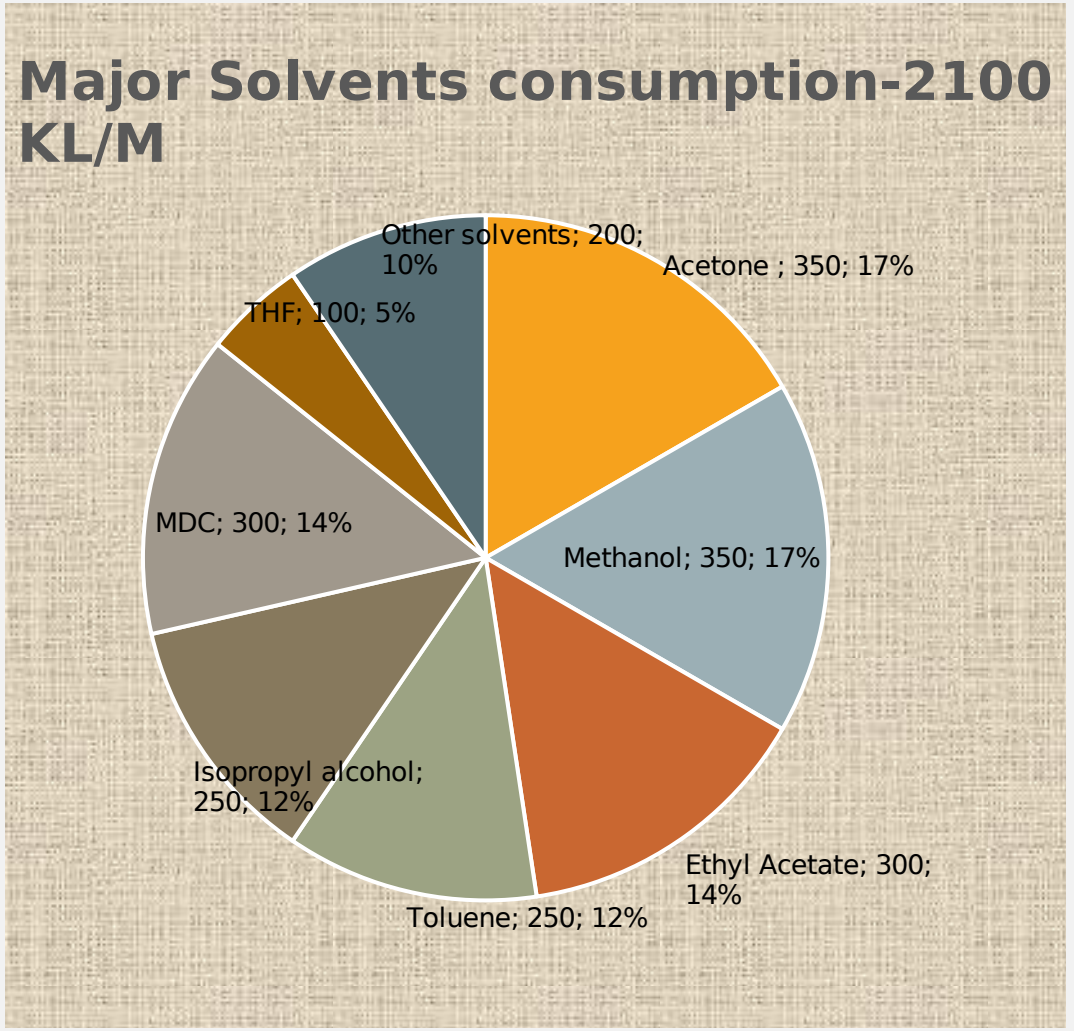
SOLVENT RECOVERY

RUDRARAM

Executive Solvents Summary in MSNL-1 Rudraram

MSNL1

Description	Quantity (KL)	Value (Cr)	Percentage(%)
Fresh solvents procurement per Annum	21600	168	--
Avg. Solvent procurement per month	1800	14.0	--
Opening stock	650	3.19	--
Inhouse Recovery	250	1.23	10
Outside Recovery	600	2.45	24
Sales	450	0.5	18
Closing stock	450	3.15	18
Losses	700	4.9	29



Out of 17.2 Cr realisation is only : ~ 7.28 Cr

We have adopted below tools to minimise the 29 % Losses

Tools

Categories

MSNL1

Control & Measure

Actions & Implementation

Realization & Sustaining

Solvent Recovery Savings initiatives

S.No	Initiatives	Actions
1	COD Reduction in effluent water	Facility needs to be created for stripping of solvents from effluent.
2	Existing solvents recovery improvements	Process optimisation and facility modifications to increase the recovery percentage & reduce the BCT
3	BOM updation in SAP	BOM revision with actual consumption of solvents
4	Segregation of solvents streams	Provided dedicated facility to avoid the cross contaminations & mixing of the solvents
5	Losses reduction in production blocks like evaporation & handling losses.	Utility changes / Condensers replacements
6	Establishment of New Distillation	Two New distillation columns commissioning

Existing Solvent Recovery System (Batch columns)

1	Existing Solvent recovery is for only batch column
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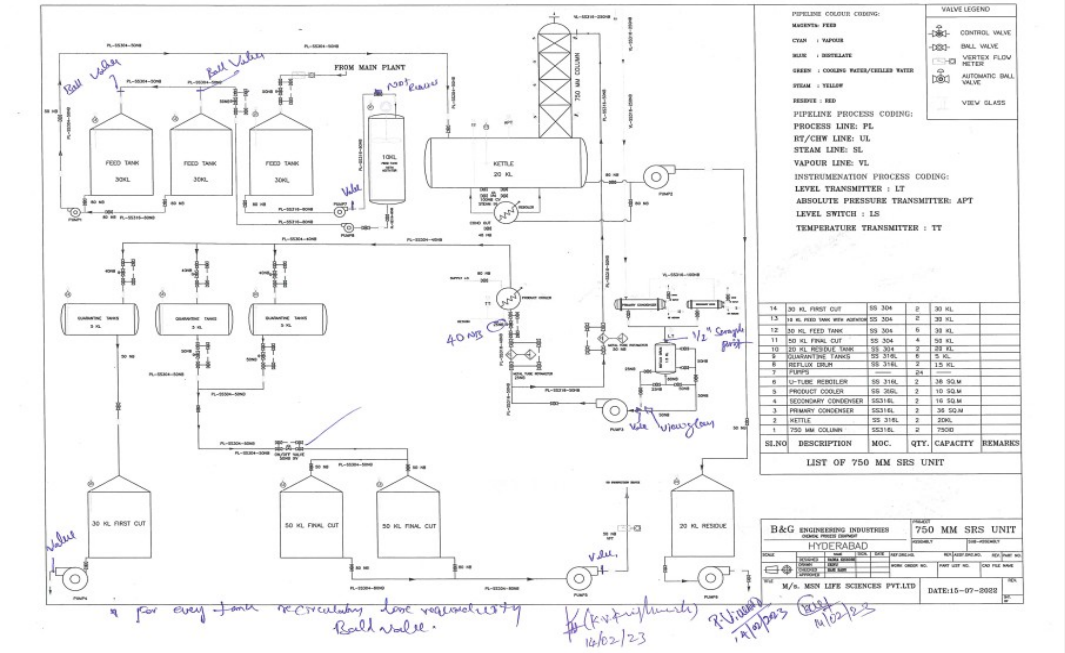

Proposed Solvent Recovery System (With Continuous top & bottom collections)

MSNL1

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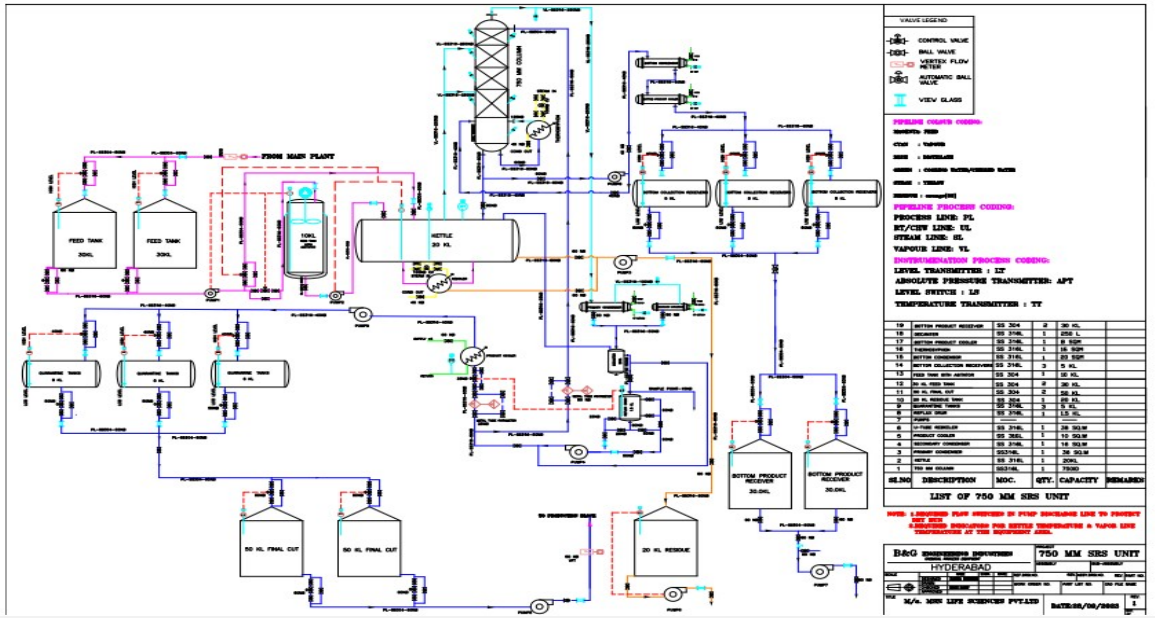
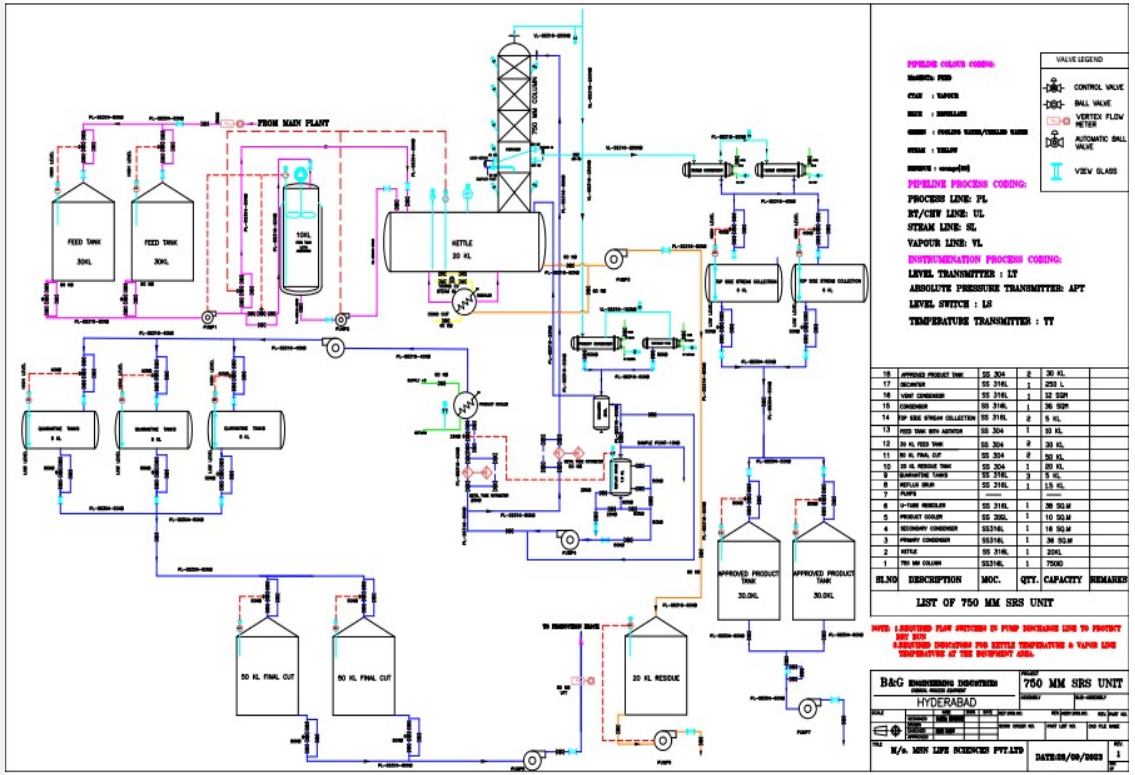
COLUMN WITH THERMOSYPHON P&ID



COLUMN WITH DOWNCOMER P&ID



Conclusions:

1	The current CAPEX cost is ~ 9 Cr for two batch distillation columns
2	By increase in 10% of Capex we can have the above stated benefits with 3 times improvement in all accepts like Safety & Productivity.

SRS ADDITIONAL INSTRUMENTATION LIST (2 COLUMNS)

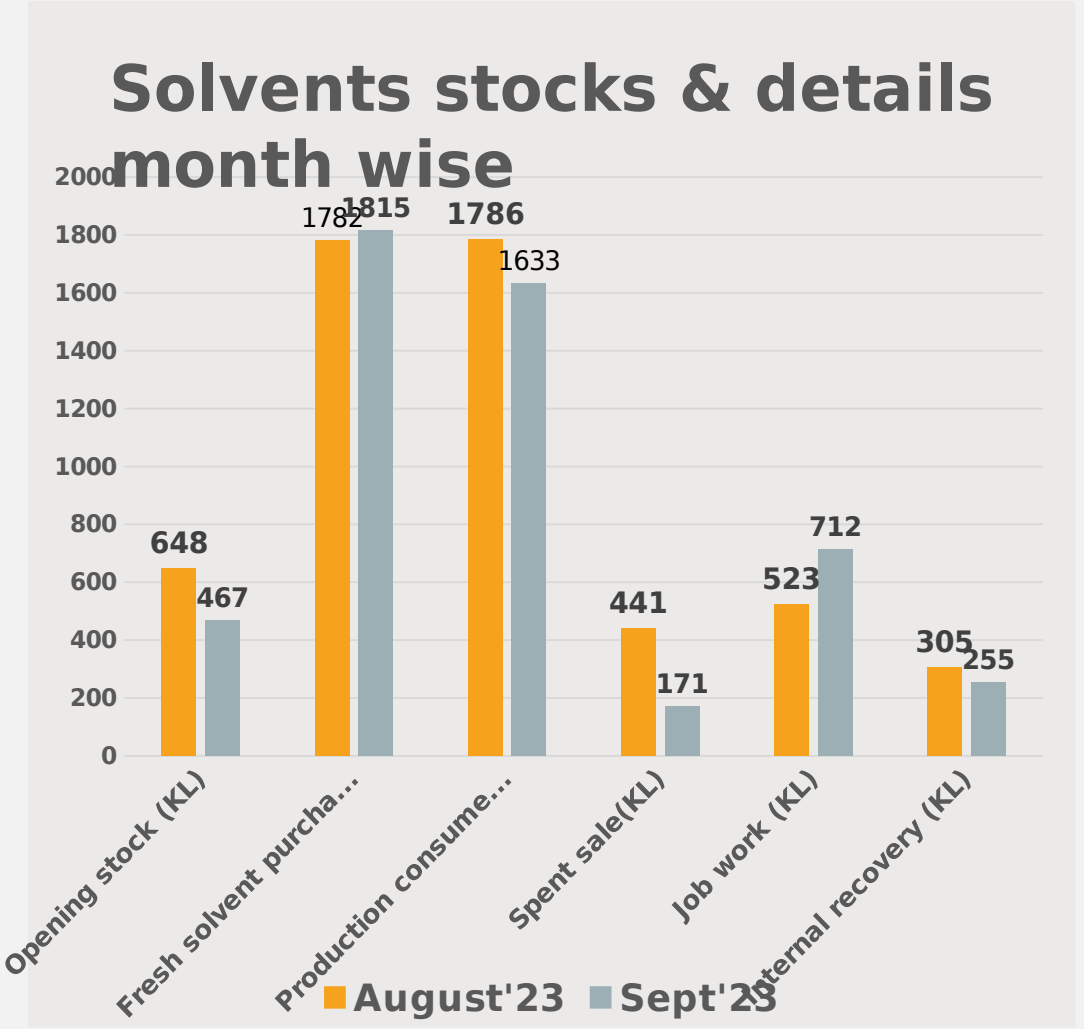
S.NO		EXISTING DESIGN	NEW PROPOSED DESIGN	VARIATION	PRICE PER EACH QTY	TOTAL PRICE
1	Automated On/off valves	18	42	24	50000	1200000
2	Flow control valves	2	2	0	0	0
3	Steam control valves	2	3	1	120000	120000
4	Level switches	20	25	5	17000	85000
5	Level transmitter	6	7	1	110000	110000
6	Metal tube rotameter	4	4	0	0	0
7	Steam flow meter	0	3	3	150000	450000
8	Vortex flow meter	4	4	0	0	0
9	Flow switches	0	18	18	15000	270000
10	Temperature transmitter	18	27	9	10000	90000
11	Pressure transmitter	6	6	0	0	0
	Total	80	141	61		2325000

MSN SRS ADDITIONAL EQUIPMENT PRICE(2 COLUMNS)

SL NO	DESCRIPTION	QTY	UOM	PRICE	
				EACH PRICE	TOTAL PRICE
1	SHELL SEGMENT FOR DOWNCOMER COLUMN	1	Nos	1,35,000	₹ 1,35,000
2	BONNET SEGMENT FOR THERMOSYPHON COLUMN	1	Nos	1,75,000	₹ 1,75,000
3	36 SQ M CONDENSER FOR DOWNCOMER COLUMN	1	Nos	10,50,000	₹ 10,50,000
4	20 SQ M BOTTOM CONDENSER FOR THERMOSYPHON COLUMN	1	Nos	6,50,000	₹ 6,50,000
5	16 SQ M REBOILER FOR THEROSYPHON COLUMN	1	Nos	5,50,000	₹ 5,50,000
6	5 KL SS316L QUARANTITE TANK	5	Nos	6,50,000	₹ 32,50,000
7	PIPE LINE & VALVES (LUMP SUM)			6,00,000	₹ 6,00,000
8	INSTRUMENTS(ON/OFF VALVES, FLOWMETERS,FLOW SWITCHES)			23,25,000	₹ 23,25,000
9	MS JACKET FOR WASHING VESSEL	2	Nos	3,00,000	₹ 6,00,000
10	12 SQM SS316L VENT CONDENSER FOR DOWN COMER	1	Nos	4,00,000	₹ 4,00,000
11	8 SQM SS316L SUB COOLER FOR THERMOSYPHON	1	Nos	3,00,000	₹ 3,00,000
12	250 LTRS SS316L DECANTER TANKS	2	Nos	2,50,000	₹ 5,00,000
13	ERECTION CHARGES			2,50,000	₹ 2,50,000
					₹ 1,07,85,000

Solvents month wise summary

Description	August'23	Sept'23	Delta	Sign
Opening stock (KL)	648	467	181	↓
Fresh solvent purchased(KL)	1782	1815	33	↑
Production consumed(KL)	1786	1633	153	↓
Spent sale(KL)	441	171	270	↓
Job work (KL)	523	712	189	↑
Internal recovery (KL)	305	255	50	↓



Updates on Solvent Recovery Savings initiatives

S.No	Initiatives	Actions	Implementations	Outcomes	Potential Savings (Lacs)	Remarks
1	COD Reduction in effluent water	Facility needs to be created for stripping of solvents from effluent.	Solvent stripping activity started in 5 KL reactor for the below streams. 1) RC1 & RC2 Columns EA Washings stripping. 2) High COD effluent from ETP 3) High Moisture process mixed streams from All production blocks.	1) Effluent water COD reduced to below ~ 0.5 lacs from ~ 6 Lacs. 2)15-20 % organic (solvents) collected from streams. 3) ~ 12KL (62 drums) Mixed solvents collected in drums	To be updated	SRS & EHS initiative
2	Existing solvents recovery improvements	Process optimisation and facility modifications to increase the recovery percentage & reduce the BCT	EA Recovery process optimisation done: 1) Optimised the Reflux ratio 2) Batch cycle time reduction 3) Recovery percentage improvement 4) First cut sale reduction - avoided	1) Avoided the first cut sale - 2500L/batch 2) BCT reduction to 30 Hrs from 55 hrs 3) Recovery percentage improved by ~12%	To be updated	SRS initiative
3	BOM updating in SAP	BOM revision with actual consumption of solvents	Initiation started in all blocks: 1) In FNR2 at C-Block: S-804 Reduced by @ 550L/Batch 2) In DGTB3A at S-Block: S-805(50% recovery usage) & S-801 Cleaning solvent reduced 3) In DGTA1A at N-Block: S-832 Solvent Qty Reduced in Isolation process S-811 Solvent Qty Reduced in workup Process	1) S-804 Reduction by 550 L/batch 2) S-805 Reduced by 2500 L/batch 3) S-801 Reduced by 100 L/batch 4) S-811 Reduced by 300 L/batch 5) S-832 Reduced by 200L/batch	To be updated	Production initiatives

MSNL1

Updates on Solvent Recovery Savings initiatives						
S.No	Initiatives	Actions	Implementations	Outcomes	Potential Savings (Lacs) MSNL1	Remarks
4	Segregation of solvents streams	Provided the dedicated facility to avoid the cross contaminations & Mixing of the solvents.	Segregation done & stored in drums: 1) PTP1 Acetone ML's 2) DEM4 Acetone ML's 3) DGTB3A Acetone ML's 4) DEM3 Cyclohexane+EA ML's 5) RBN5 IPA ML's 6) OMX5 MDC+Acetone ML's	1) PTP1 Acetone ML's - To be sent for Job work 2) DEM 4 Acetone ML's - Sent for Job work 3) DGTB3A Acetone ML's - To be sent for Job work 4) DEM3 Cyclohexane+EA ML's - To be sent for job work 5) RBN5 IPA ML's - To be sent for Job work 6) OMX5 MDC+Acetone ML's - Sent for Job work	To be updated	EMS & TSD initiatives
5	Losses reduction in production blocks like evaporation & handling losses.	Utility changes / Condensers replacements	Utility changes done in condensers for MDC,THF distillations.	1) VGB1 at N block - SSR23 & 29 Uitility changed with +5, (THF,MDC) 2) VGB1 at R block - SSR22 & 32 Uitility changed with +5, (THF,MDC) 3) Duloxitine at P block - SSR2 Utility changed with +5 (MTBE)	To be updated	TSD initiatives
6	Establishment of New Distillation columns	Two New distillation columns commissioning	Civil structure work under progress & Systems will be engaged for IPA,EA,Toluene,Acetone, THF & for other solvents	1) Two Distillation column's p&id's finalised with bo`ttom collection & downcomer facility 2) Need to discuss with vender for safety & process controls - Automisation	To be updated	SRS initiative

THANK YOU

Technical Services

Department,
Organics

TSD –Quarterly Review

- Safety Improvement
- Quality Improvement of Etifoxine
- New Product Update
- Capacity Improvement
- Design Improvements

Etifoxine Manganese Dioxide Charging Safe Handling

MSN Organics Private Limited

Proposal

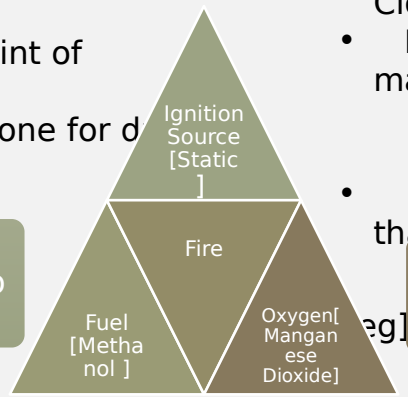
oxine is manufactured in D-Block campaign basis product (600kg /annum) with revenue 1.5Cr, currently Manganese Dioxide being used for cyclization by inse

ing Procedure : Currently the Manganese Dioxide [52kg] shall be charged in to reactor in 500L methanol through Manhole with Scoop with Nitrogen blanket

Current Procedure :

- Charging of material through manhole , Risk of Air exposure.
- No Positive Nitrogen atmosphere
- Charging of Manganese dioxide above the flash point of methanol
- Particle size of Manganese dioxide is 44 micron , prone for d cloud

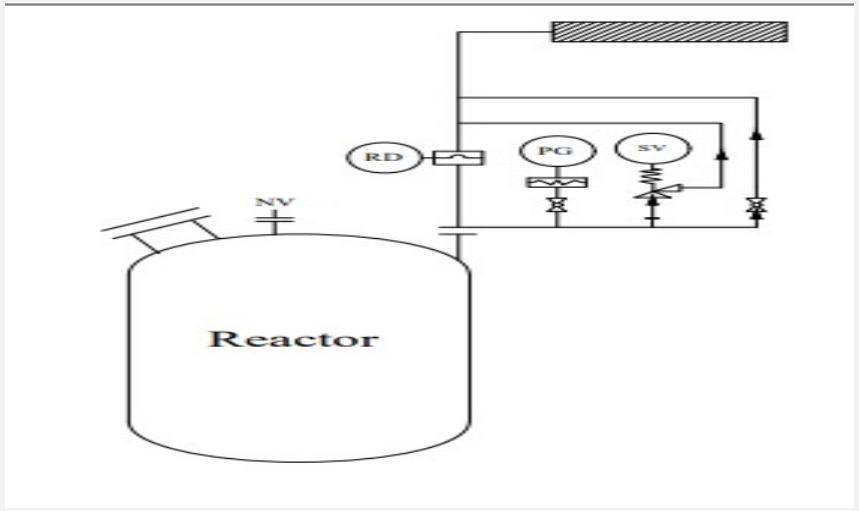
Mangan ese Dioxide Chargin g → Above the Flash Point of Solvent → No Complet e Blanketi ng → Un Safe Conditio n

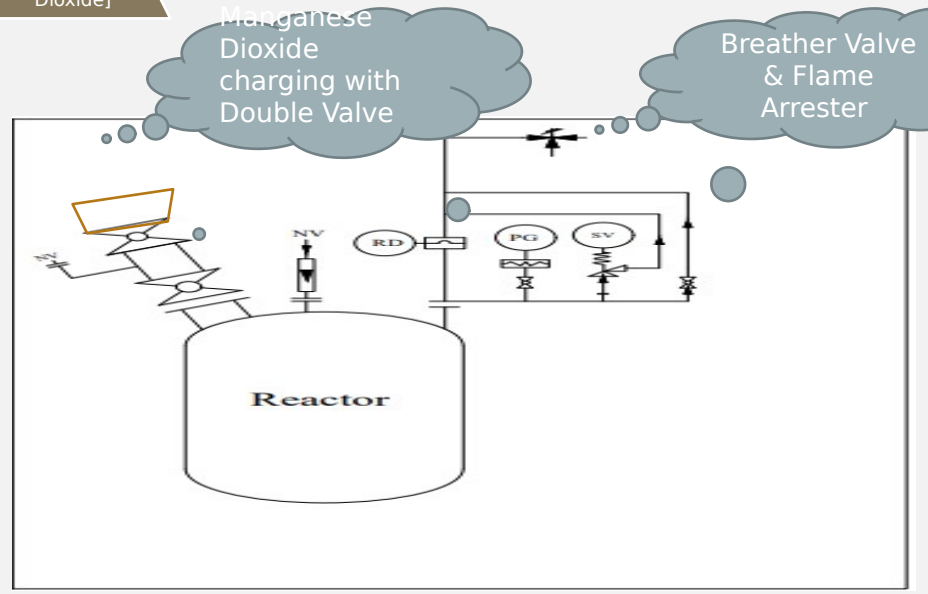


Opportunity :

- Double Valve system to charge the Manganese Dioxide in Close condition.
- Provision of Breather Valve with Flame arrester in vent manifold to keep 200mmwc Positive nitrogen Blanketing during the material charging.
- Reducing the charging temperature from 30-35 deg to less than 10 deg to

Manganese Dioxide Charging → Less than Flash Point of Solvent → Nitrogen Positive Atmosphere → Safe Handling





P&ID

Cos t 0.5 Lac

New Products – Fosfomycin

Tromethamine

Current Update

Innovator: Zambon Spa Italy
Brand Name:Monurol
Dosage Form: Oral/20mg/day
Therapeutic Category: Antibiotic

Stage-1 FSM3A
[Input 150Kg ,
Out Put /Bz -189 kg {73.8%}
Nos of batches-15
4/15 batches completed.
Kilo Lab : Input 7Kg , Out put 7.11 Kg 1.02w/w{58%}

Stage-2 FSM4A
[Out Put /Bz -50 kg
Nos of batches-15
TT Planned-
1st Week of OCT-23

Stage-3 -API
[Out Put /Bz -90 kg
Nos of batches-4
TT Planned Last week of Oct-23

Stage-1 :Target for completion Mid Nov-23

Stage-2 Target by End of Nov-23

Stage-3 :Target 2nd week of Dec-23

Highlights of Stage-3A:

Theoretical Assessment of Hydrogenation Heat of Reaction with Group Contribution Method .[

The Product is UV in-active , we understood the parameters for 3 conversions and scale up done with consistent yield.

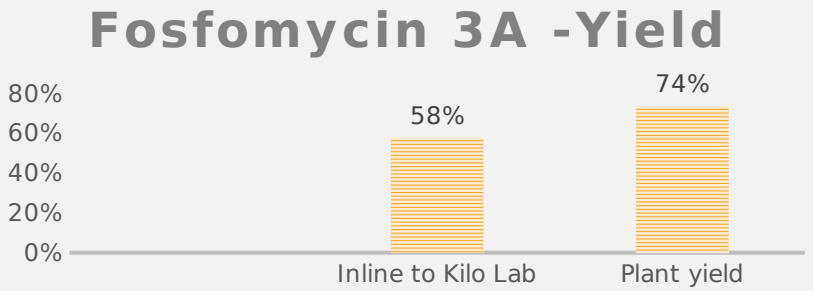
Consistent Yield and Quality.

Closed system for Key Reagents addition.

Higher Yield (26% than Kilo Lab .

Validation planned with 2 Hydrogenators

Dehumidification set up designed for API Drying



Heat of Reaction –Hydrogenation –From Bond Energy

	SM	H2	Product
Mwt	232	2	234
Batch size			
Heat of Formation (KJ/mole)	-1090.88	218	-1259.19
Number of Moles as per balance equivation	1	1	1
Heat of Reaction	-386.31	KJ/mole	
Heat for 150Kg Batch	256.2044	Kg	
Total Heat load during Reaction	-98974.3	KJ	
	-23565.3	Kcal	
Reaction mass Prior Hydrogenation	1200	Kg	
PCL3 Mwt	137	Kg	
Batch size PCL3	150	Kg	
Theoritical Product	256.2044		

Heat of Reaction

Theoretical Adiabatic Temperature raise is 19.6 deg

New Products – Tapinarof

Current Update

TPNK-1
Input : 44 Kg
[Out Put /Bz -46.6 kg
5/5 batches completed
Plant Yield : 1.08w/w {83%}
[Kilo lab 0.89w/w-65w/w]

TPNK-2
Input : 45 Kg
[Out Put /Bz -36.6 kg
5/5 batches completed
Yield : 0.81w/w {71%]
[Kilo lab 0.79w/w{69%]

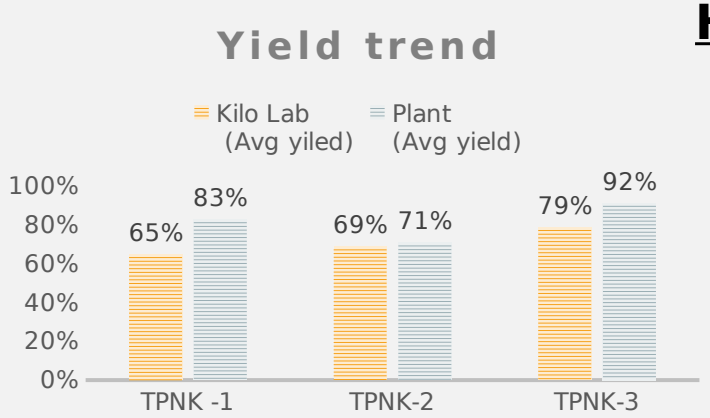
TPNK-3A
Input : 36 Kg
[Out Put /Bz -33.75 kg
2/5 batches completed
Yield : 0.87w/w {91.7%& 922.7]
[Kilo lab 0.74w/w{79%]

Stage-4A[TT 17th Sept 23]
Stage-7A [8th Oct23]
Stage-8A [API] TT shall be planned [17th Oct23]

Tapinarof Batch details

Tapinarof Schedule

Innovator: Dermavant Sciences
Brand Name: VTAMA
Dosage Form: Cream/600mg/day
Therapeutic Category: psoriasis



Highlights Projects:

TPNK-2 : Dimer impurity is controlled less than <0.09 % against 0.5% of Kilo Lab trend with Temperature controller in Hot water system

Closed system for Borohydride , BF3 etharate addition with double valve and Paraffin trap.

All Stages yield are higher than Kilo lab.

Consistent Yield and Quality.

TPNK-1 Completed Sept-23

TPNK-2 under Last batch of the campaign

TPNK3A , Target for completion by OCT-23

Heat of Reaction From Group Contribution Method

Summary of Tapinarof BF3 Etharate Theoretical Heat of Reaction from Bond energy

	SM	NaBH4	BF3	Product	Diborane	NaBF4
Mwt	224.25	37	37	234	27.6	41
Batch size			298	302.6		
Heat of Formation (KJ/mole)	-897.95	-192	-269.	-566	36	-1845
Number of Moles as per balance equivation	1	1	1	1	1	1
Heat of Reaction	-1015.17	KJ/mole				
Heat for 33 Kg Batch	33.75	Kg				
Total Heat load during Reaction	-34262	KJ				
	-8157.62	Kcal				
Reaction mass Prior BF3 Addition	198.49	Kg				
BF3 Mwt	37	Kg				
Batch size	36	Kg				
Theoritical Product	33.75					
ΔT adibatic (Theoritical from Bond energy)	-41.0984	deg				

F3 Etharate hea of Reaction

Theoretical addition Time -4hrs

New Products – Belmusodil

Current Update

BLSC-1/BSDM2A
Input : 25Kg
[Out Put /Bz -41.45 kg
4/4 batches completed
Plant Yield : 1.66w/w {80.5%}
[Kilo lab 1.61w/w- [78%]

BSDB-2(Fragment-B)/ BLSB1
Input : 23 Kg
[Out Put /Bz -21.3 kg
2/5 batches completed
Plant Yield : 0.92w/w {70%}
[Kilo lab 0.80w/w{57%]

BLSC-2/BSDM3A-Fragment-C
Input : 39 Kg
[Out Put /Bz -33.87 kg
4/4 batches completed
Plant Yield : 0.87w/w {82%}
[Kilo lab 0.84w/w- [79%]

BLSM-1 (B+C)
Input : 23 Kg
[Exp Out Put /Bz -18.8kg
1/4 batches -Trial Batch U/P
Plant Yield :
[Kilo lab 0.82w/w{79%]

BSDA2A(Fragment A)
Input : 15Kg
[Expected Out Put /Bz -25 kg
Execution planned in OCT-23

BLSM-2 (Fragment-A+BLSM-1)
TT Shall be planned

API

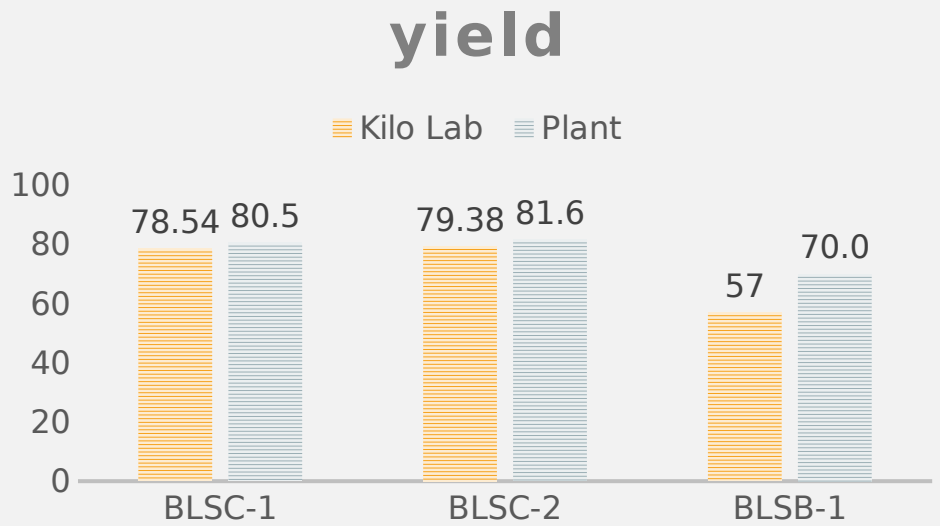
Innovator: Kadmon Pharmaceuticals
Brand Name: Rezurock
Dosage Form: 200mg/day
Therapeutic Category: Treat graft versus host disease

Highlights Projects:

Consistent yield

BLSB-1 Distillation time optimized and Yields improved from 78% to 92% [18Kg to 21.3Kg] .

Raney Nickle Filtration done with leaf filter instead of conventional decantation ,will have huge time cycle reduction on catalyst filtration and safety improvement on handling perspective.

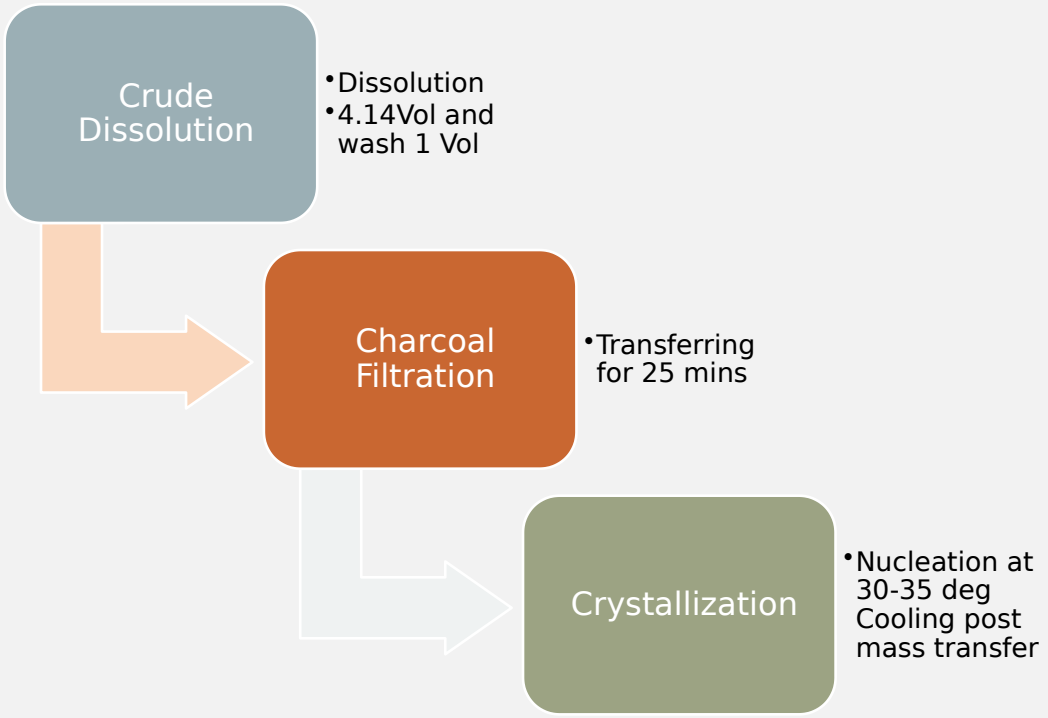


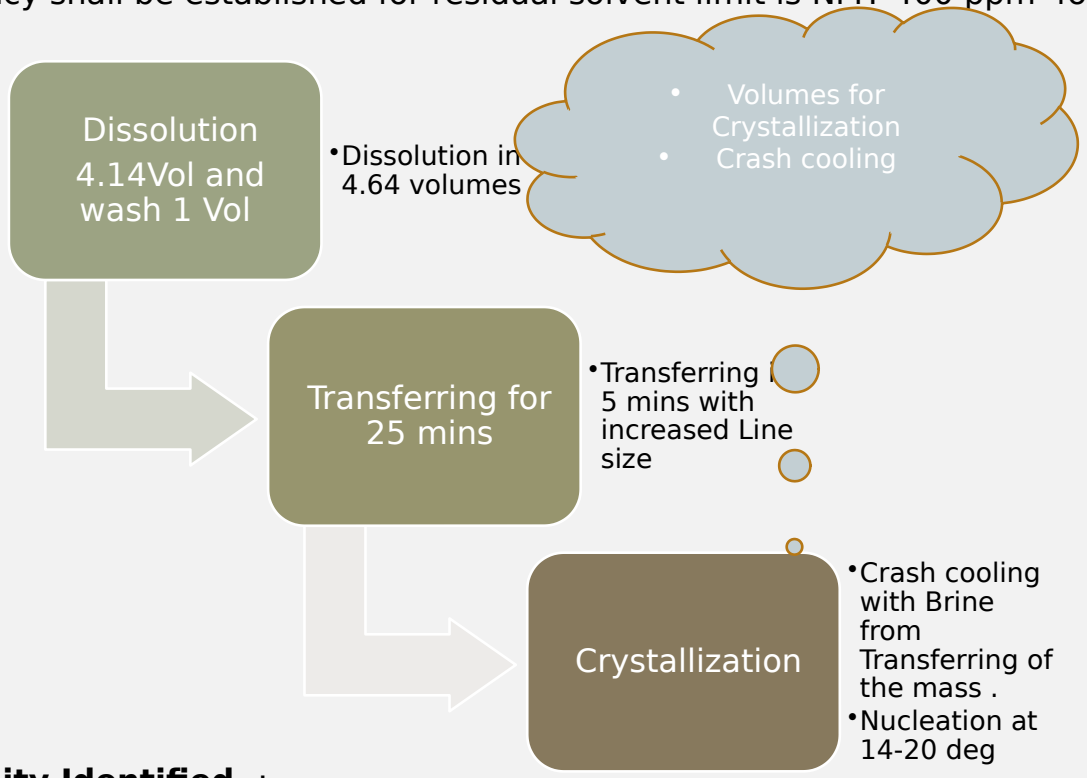
Etifoxine Acetonitrile OVI Consistency Establishment with Crystallization

MSN Organics Private Limited

Existing : Etifoxine is manufactured in D-Block campaign basis product (600kg /annum) with revenue 1.5Cr, currently Manganese Dioxide being used for cyclization by insertion of oxygen.

Robustness Required : Currently API is crystalized with Acetonitrile ,consistency shall be established for residual solvent limit is NMT 400 ppm for 610 Kg dispatch of Sept23 targets (1.5Cr) with crystallization




Dissolution 4.14Vol and wash 1 Vol
•Dissolution in 4.64 volumes
• Volumes for Crystallization
• Crash cooling
Transferring for 25 mins
•Transferring for 5 mins with increased Line size
Crystallization
•Crash cooling with Brine from Transferring of the mass .
•Nucleation at 14-20 deg

Current Procedure :

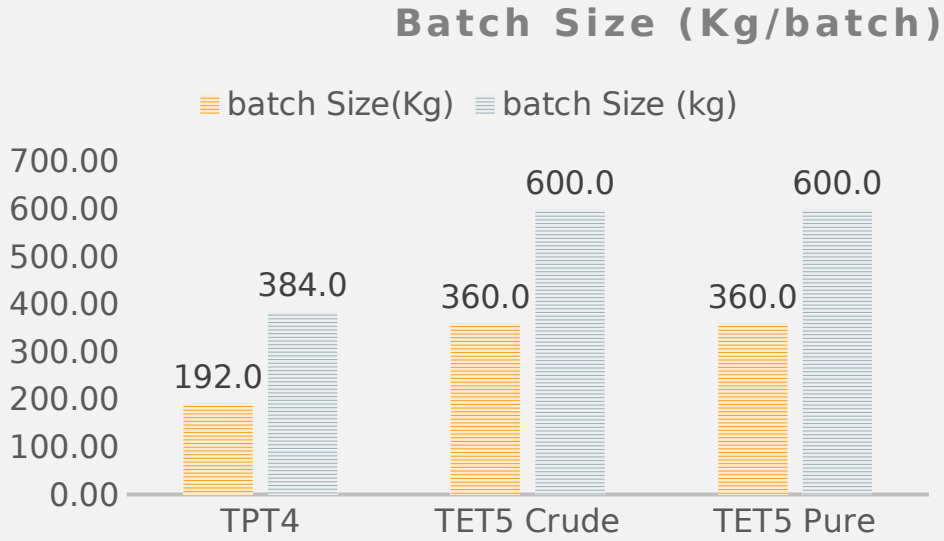
- Crude /Pure dissolved in 4.14 vol of Acetonitrile at 50-60 deg.
- Charcoal washing is 1 Vol
- Coarser material observed when nucleation observed at 30 -35 deg .
- 4-5 Kg material loss observed for delay of transfer for about 30mins , due to lesser size pump suction [25 NB for 12 M3/hr pump] .

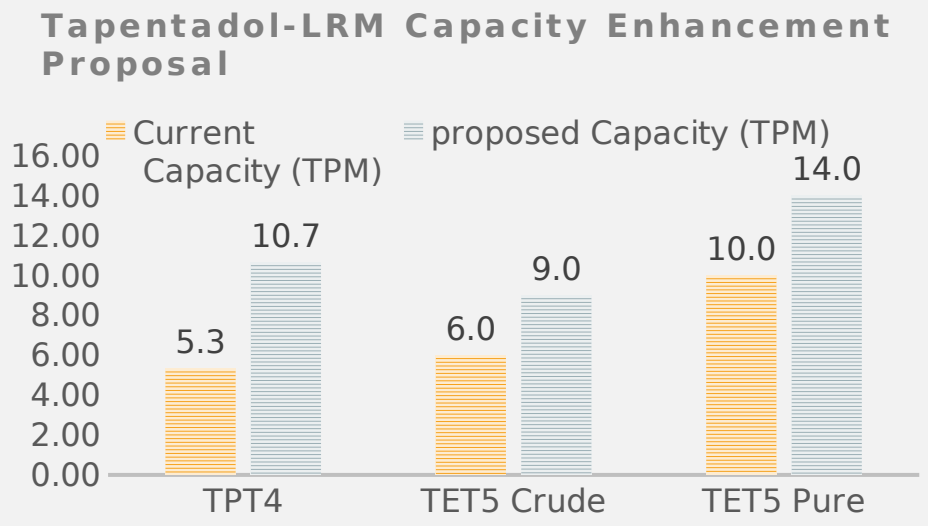
Opportunity Identified :

- Crude dissolved in 4.14 volumes at 50 deg and agitator stopped to avoid product degradation to olefin impurity .
- Crystal bulk density and size verified with crash crystallization with 5.14 V and 4.64 volume. 4.64 volumes consistently given fine crystals particle with <200 ppm Acetonitrile .
- Pump suction increased to 40 NB and Transferring completed within 5 mins and washing 2 mins . Reduced exposure time yield 4-5 kg more output than historical trend.

Capacity Assessment-Tapentadol LRM 5TPM to 9TPM

MSN Organics Private Limited





- TET-4 Batch size enhancement done progressively from 192 kg to 384 Kg [384kg U/P] in 3KL Hydrogenator.
- 1.2KL Hydrogenator re-mapped with 2KL SSR in A-Block to declash the Hydrogenator and use for Fosfomycin and other products for TET-4 TFA Reaction.
- Diasteromer impurity is under control .
- Water volumes for TET-5 works eliminated by Lab experiments and under implementation.

- Capacity enhancement from 2TPM to 4TPM working for RM under progress with time cycle and batch size optimization.

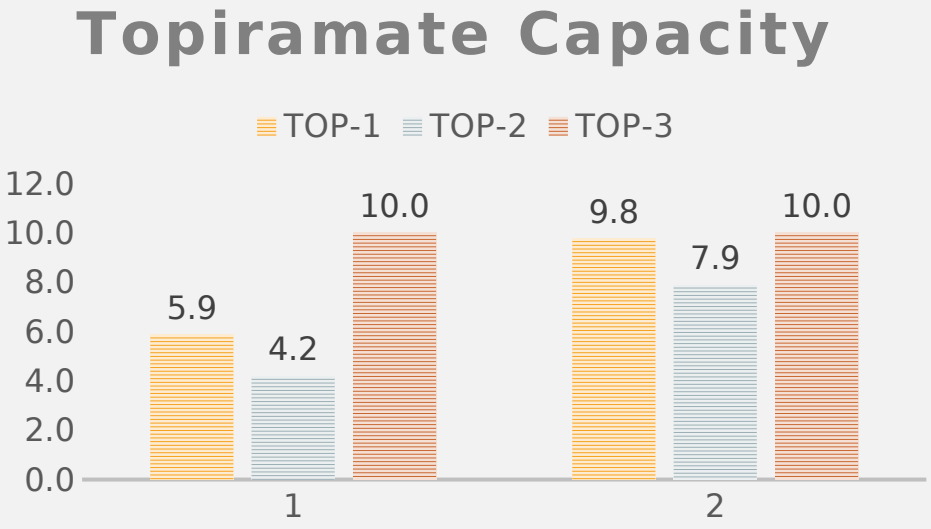
Tapentatol LRM Capacity

Tapentatol RM Capacity

Capacity Assessment- Topiramate 4TPM to 8TPM

MSN Organics Private Limited

Stage	Current (TPM)	Proposed (TPM)-1 with existing Equipment and time cycle optimization	Inline to Remarks with additional equipment's	Equipment's Usage Elimination to Improve Tapentadol Capacity	Remarks
TOP-1	5.9	4.9	9.8	8KL SSR Excluded - SSR15 , shall be planned for Tapentadol . Salt Filtration shall be planned with Decantation to Eliminate ANFD-01 and same shall be planned for Tapentatol.	Adding 5KL SSR will increase the capacity up to 9TPM
TOP-2	4.2	5.9	7.9	GLR/23 -4Kl -used for sulphuryl chloride solution preparation shall be spare for other products. Reaction time cycle reduced with increased area of Ammonia sparer(Dual sparger)-8hrs	Shall increase 2MT with 5KL GLR and 5KL SSR additional steam as parallel stream.
TOP-3	10.0	10.0	10.0	Validated in 6KL and 4KL Crystallizer . Shall be planned with 4KL Crystallizer E2 and 6KL Crystallizer for other products	



Topiramate Capacity

- Capacity enhancement from 4TPM to 8TPM working with time cycle and batch size optimization.
- 4KL GLR ,8KL SSR and 2KL ANFD capacity released for Tapendatol Capacity improvement

Safety Improvements – Proposals

MSN Organics Private Limited

Sr.No	Activity	Category	Summary	Status	Remarks
1	Manganese Dioxide handling system for Etifoxine to mitigate the Fire Hazard	Safety	➢ Charging with double valve hopper ➢ Nitrogen blanketing with breather valve ➢ Material charging below the flash point of methanol.[,11 deg]		Implemented Etifoxine Mno2 Handling
2	Drum transfer system	Safety	Pipe in Pipe system Implemented for fosfomycin TEA addition . PCl3 handling done with AODD Pump under closed system.		Drum handling.mp4
3	Scrubber Catch pot for HBr gas	Quality/ Safety	The Double Catch pot system will be prevent the HBr direct loss and scrub the vented gas from the system . P&ID attached. Movable double catch pot system planned as proof of concept for PCL3 for Fosfomycin , once established ETFE lined pots will be planned for HBr.		Gas Scrubbing P&ID
4	Ammonia Layer Separation in F Block	Safety/ Producvity	Layer separations handling will have Ammonia exposure inside the Block . Tanks under procurement- TCD-OCt23		Tanks expected to Site by Next week . Planned installation Oct-23
5	Intertization System for Centrifuge	Safety	Planned for MLPL-2 centrifuges		

Notes : Under Progress | To be initiated | Completed | Needs Approval

Design Improvements - Organics

MSN Organics Private Limited

Sr.No	Activity	Category	Summary	Status	Remarks
6	Efficient heat exchangers for MEPL-2 new Site	New Technology / Efficiency	Conventional to Corrugated Heat exchanges implementation planned for 2 Reactor [4 condensers] . Other 18 No's drawing review completed and handover to Tilak for necessary approval		Planned for AppliChem B-Block
7	pH Sensors Frequent Damage	Design Improvement	pH meters shall be planned in Pump re-circulation with U-seal to avoid the dryness and solid deposition		Cost 40000 Rs [Approved} Sensors Received , shall be installed inline Proposed P&ID to avoid the frequent damage.
8	Cooling Tower Fan Cut off with Temperature	Energy Savings	Proposal approved , shall be planned for 1-2 cooling tower for performance assessment		Set up fixed , Energy Meters under installation for assessment.
9	Particle size reduction of Dimethyl Fumarate with Wetmill	New technology	PSD trials completed with Ystral and meeting for DMF and Tadalafil PSD D90 up to 17 Micron ,requirement is < 10 Micron. Planned trials with flow cell in OCT-23		Quote Received from Bectochem for similar model [40 Lac]
10	MLPL-2 Existing Cooling Tower usage for New Block to Save the Capital Investment	Design	Assessed the heat Load with additional vaccum pumps ,found existing 200TR will be suffeient to handle the load.		Investment Savings -471.15 Lac

Notes : Under Progress | To be initiated | Completed | Needs Approval

Design Improvements -Organics

MSN Organics Private Limited

Sr.No	Activity	Category	Summary	Status	Remarks
10	Requirements for Japan – Extraneous matter control	Facility	Team discussion with all functions and actions concluded for standardization.		tequirements for Japan
11	Vacuum Pumps assessment	facility	Vacuum Pump Design & Handling basis concluded for distillation, Filtration and Drying Operations.		vaccum pumps basis
12	Energy efficient agitators	Design Improvement	Energy efficient Agitators , Planned for APIchem 1KL to 3KL Reactors considering the multi Product mix requirements		Energy Effeceint Agitators
13	Nitrogen Compressor Noise in Engineering and TSD working area	Design Improvement	Exhaust Line size Increased from 3” to 6” and Line extended out the Engineering Block , noise levels		

Notes : Under Progress | To be initiated | Completed | Needs Approval

Nitrogen Compressor Noise

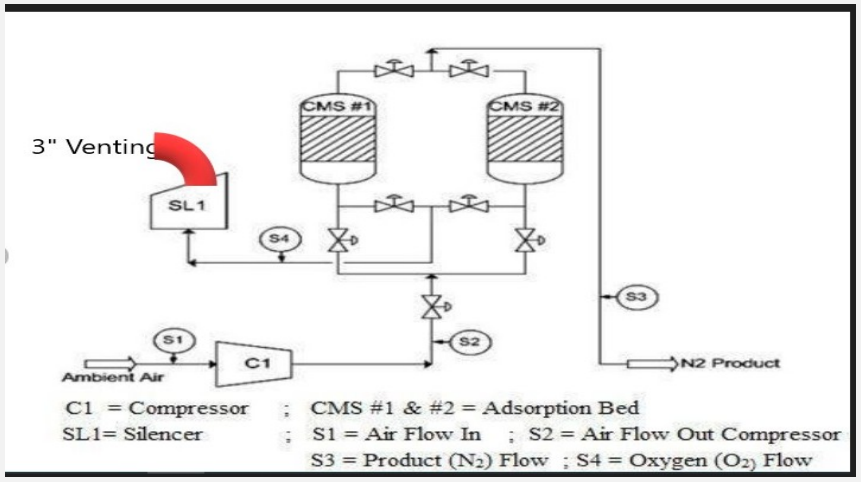
MSN Organics Private Limited

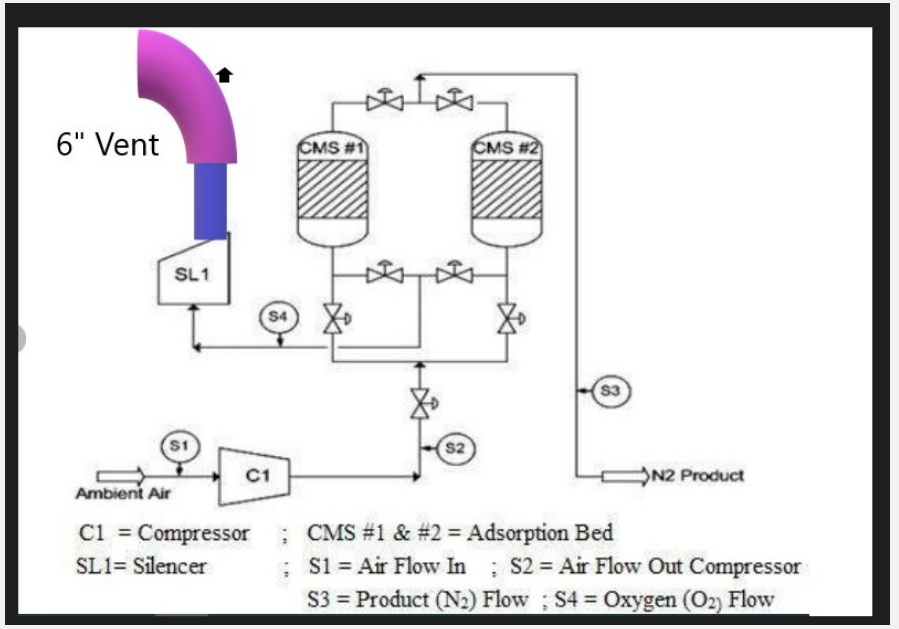
Problem Statement:
We have 50Nm3/hr Nitrogen system is installed in utility area and the rejected oxygen flow is discharged from Silencer with 3" Vent pipe .
Loud Noise observed in office area of Engineering and TSD ,due to high velocity discharge .

Theory of Noise Impact :
The average person is born with about 16,000 hair cells within their cochlea. These cells allow your brain to detect sounds. Up to 30% to 50% of hair cells can be damaged or destroyed before changes in your hearing can be measured by a hearing test.However, if loud noise damaged too many of the hair cells, some of them will die. Repeated exposures to loud noises will over time destroy many hair cells. This can gradually reduce your ability to understand speech in noisy places. Eventually, if hearing loss continues, it can become hard to understand speech even in quieter places.

Noise Can Also Damage Nerves in Your Ears
In addition to damaging hair cells, noise can also damage the auditory nerve that carries information about sounds to your brain. Early damage may not show up on your hearing test. It can create a 'hidden hearing loss' that may make it difficult for you to understand speech in noisy places. The effect of loud noise over time affects how well you might hear later in life. It also affects how quickly you might develop hearing problems, even after exposure has stopped.

Short term Actions taken taken for Exhaust System :
Discharge silencers should be maintained below 150ft/sec velocity . The exhaust end of the silencer should be free from reflective surfaces and avoided inside .
Since the silencer was inside , to reduce the reflective noise the exhaust is expanded and extended outside the area.





MLPL-2 Ejector Cooling Tower Savings by Usage of Existing

MSN Organics Private Limited

S.No	Equipment Description	Qty	Uom	Unit Cost	Total Cost
1	Civil Structure with Sump	Lum		3400000	3400000
2	Electrical requirements	Lum		500000	500000
3	Pipes and fittings with Traps	Lum		600000	600000
4	SteamJetEjectorVacuum Combin Pump 320m3/Hr	2	No's	520000	1040000
5	SS316 360 m3/hr Water Ring Vacuum Pump	5	No's	290000	1450000
6	200 TR Cooling tower	1	no's	275000	275000
					7265000

The existing ejector cooling tower is of 200TR capacity and having 5 water ring pumps and 2 water ejectors without steam.
In principle steam jet ejector will have 20TR load and water ring load is negligible 1-2 TR. Hence currently no major load on the running system .
Considering the same , instead of purchasing the new ejector cooling tower ,we can utilize the existing cooling tower for additional water ring pumps .

Ejector Cooling
r Investment Sa

Investment Savings 47.15 Lacs

Thank You